

## WEST Search History





DATE: Monday, February 07, 2005

Hide?	<u>Set</u> <u>Name</u>	<u>Query</u>	<u>Hit</u> <u>Count</u>
	<i>DB=PGPB,USPT; PLUR=YES; OP=OR</i>		
<input type="checkbox"/>	L17	(inlet or outlet) and l6	1
<input type="checkbox"/>	L16	inlet or outlet and l6	468833
<input type="checkbox"/>	L15	TGGE and 20050014163.pn.	1
<input type="checkbox"/>	L14	20050014163.pn.	1
<input type="checkbox"/>	L13	((thermic or thermal or thermically or thermally) near5 gradient) same (DNA or protein)	367
<input type="checkbox"/>	L12	((thermic or thermal or thermically or thermally) near5 gradient) and (DNA or protein)	1040
<input type="checkbox"/>	L11	(thermic or thermal or thermically or thermally) near5 gradient	12998
<input type="checkbox"/>	L10	(thermic or thermal) near5 gradient	12789
<input type="checkbox"/>	L9	therm\$ near5 gradient	13836
<input type="checkbox"/>	L8	l5 and l7	1
<input type="checkbox"/>	L7	target same protein and l6	1
<input type="checkbox"/>	L6	20030077599.pn.	1
<input type="checkbox"/>	L5	(thermophoresis or thermophoretic) same protein	1
<input type="checkbox"/>	L4	(thermophoresis or thermophoretic) same protein	1
<input type="checkbox"/>	L3	(thermophoresis or thermophoretic) and protein	17
<input type="checkbox"/>	L2	(thermophoresis or thermophoretic) AND DNA	6
<input type="checkbox"/>	L1	(thermophoresis or thermophoretic) same DNA	2

END OF SEARCH HISTORY

## WEST Search History

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DATE: Monday, February 07, 2005

Hide?	<u>Set</u> <u>Name</u>	<u>Query</u>	<u>Hit</u> <u>Count</u>
		<i>DB=PGPB,USPT; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L5	DNA and l3	1
<input type="checkbox"/>	L4	l1 and L3	0
<input type="checkbox"/>	L3	sogard-m\$.in.	39
<input type="checkbox"/>	L2	((thermic or thermal or thermically or thermally) near5 gradient) same (DNA or protein) same (array or microarray)	8
<input type="checkbox"/>	L1	((thermic or thermal or thermically or thermally) near5 gradient) same (DNA or protein)	367

END OF SEARCH HISTORY

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NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	JAN 26	CA/CAPLUS - Expanded patent coverage to include the Russian Agency for Patents and Trademarks (ROSPATENT)
NEWS EXPRESS	JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005		
NEWS HOURS	STN Operating Hours Plus Help Desk Availability		
NEWS INTER	General Internet Information		
NEWS LOGIN	Welcome Banner and News Items		
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN		
NEWS WWW	CAS World Wide Web Site (general information)		

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=> fil medline biosis caplus embase wpids'

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0.21	0.21

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FILE 'MEDLINE' ENTERED AT 15:22:26 ON 07 FEB 2005

FILE 'BIOSIS' ENTERED AT 15:22:26 ON 07 FEB 2005

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FILE 'CAPLUS' ENTERED AT 15:22:26 ON 07 FEB 2005

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FILE 'WPIDS' ENTERED AT 15:22:26 ON 07 FEB 2005

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=> e sogard m/au

MISSING TERM FOR FIELD QUALIFICATION BEFORE '/AU'

The search profile entered contains a field qualifier, e.g., '/AU', with no term preceding it.

=> e sogard m/au

E1	1	SOGARD J/AU
E2	1	SOGARD JORGENSEN R/AU
E3	28 -->	SOGARD M/AU
E4	41	SOGARD M R/AU
E5	8	SOGARD MICHAEL/AU
E6	12	SOGARD MICHAEL R/AU
E7	4	SOGARD P/AU
E8	2	SOGARD S/AU
E9	17	SOGARD S M/AU
E10	22	SOGARD SUSAN M/AU
E11	2	SOGARI F/AU
E12	1	SOGARI FRANCESCO/AU

=> e3-e6

L1 87 ("SOGARD M"/AU OR "SOGARD M R"/AU OR "SOGARD MICHAEL"/AU OR "SOGARD MICHAEL R"/AU)

=> l1 and ?therm?

L2 11 L1 AND ?THERM?

=> dup rem l2

PROCESSING COMPLETED FOR L2

L3 8 DUP REM L2 (3 DUPLICATES REMOVED)

=> l3 and DNA

L4 1 L3 AND DNA

=> d ibib abs l4

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:319338 CAPLUS  
DOCUMENT NUMBER: 138:298809  
TITLE: Methods and devices for improving hybridization  
stringency of microarrays using **thermophoresis**  
INVENTOR(S): **Sogard, Michael**  
PATENT ASSIGNEE(S): Nikon Research Corporation of America, USA  
SOURCE: U.S. Pat. Appl. Publ., 12 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
US 2003077599	A1	20030424	US 2001-38342	20011023
PRIORITY APPLN. INFO.:			US 2001-38342	20011023

AB An apparatus and method for performing hybridization or binding assays under **thermophoretic** conditions is provided. In particular, it relates to improving the hybridization stringency or decreasing the time required for hybridization in microarrays using **thermophoresis**. The apparatus for performing hybridization comprises a container connected to at least one temperature control block in a heat-conducting fashion, such that a temperature gradient is produced and contains inlet and outlet ports and optical access to the container via an aperture. Temperature gradients may be between 5-25 °C and the array may have a d. between 10,000 to 1 million probes per square cm.

=> l3 not l4

L5 7 L3 NOT L4

=> t ti l5 1-7

L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
TI Wafer heating analysis for electron-beam projection lithography

L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
TI Method and device for controlling **thermal** distortion in elements of a lithography system

L5 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
TI Periodic clamping method and apparatus to reduce **thermal** stress in a wafer

L5 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
TI Optical inspection of EPL stencil masks

L5 ANSWER 5 OF 7 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN  
TI Extreme ultraviolet apparatus has mirror including conduit provided inside channel for conducting cooling fluid, and gap is formed between conduit and channel such that low pressure is maintained in gap.

L5 ANSWER 6 OF 7 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN  
TI Electrostatic chuck has hollow area between multilayered membrane and support unit, and is connected to cooling gas supply source through gas piping holes on support unit.

L5 ANSWER 7 OF 7 WPIDS COPYRIGHT 2005 THE THOMSON`CORP on STN  
TI X-Y stage for machine tool used in lithography for semiconductor wafer processing has spaced bearings extending from a bottom of the stage plate and each having an arcuate bottom in contact with the surface of the base plate.

=> (thermic or thermal or thermically or thermally) (s) gradient  
L6 11990 (THERMIC OR THERMAL OR THERMICALLY OR THERMALLY) (S) GRADIENT

=> (DNA or protein) and (array or microarray)  
4 FILES SEARCHED...  
L7 90771 (DNA OR PROTEIN) AND (ARRAY OR MICROARRAY)

=> l6 and l7  
L8 15 L6 AND L7

=> (thermophoresis or thermophoretic) and l7  
L9 1 (THERMOPHORESIS OR THERMOPHORETIC) AND L7

=> l9 not l4  
L10 0 L9 NOT L4

=> l8 not l4  
L11 15 L8 NOT L4

=> t ti l8 1-15

L8 ANSWER 1 OF 15 MEDLINE on STN  
TI **DNA** mutation detection in a polymer microfluidic network using temperature gradient gel electrophoresis.

L8 ANSWER 2 OF 15 MEDLINE on STN  
TI Genotyping on a **thermal gradient DNA** chip.

L8 ANSWER 3 OF 15 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN  
TI Methodologies for the characterization of microbes in industrial environments: A review.

L8 ANSWER 4 OF 15 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN  
TI Genotyping on a **thermal gradient DNA** chip.

L8 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN  
TI Analysis of point mutations by **array** hybridization, **thermal gradient** denaturation and total internal reflection fluorometry

L8 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN  
TI **DNA** Mutation Detection in a Polymer Microfluidic Network Using Temperature Gradient Gel Electrophoresis

L8 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN  
TI Genotyping on a **thermal gradient DNA** chip

L8 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN  
TI Surface modification and hybridization on a **thermal gradient DNA** chip

L8 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN  
TI Apparatus for generating a temperature gradient and methods for using the

gradient to characterize molecular interactions

- L8 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN  
TI A device for detecting specific hybridization in microarrays using temperature gradients and imaging of hybridizations labeled with a reporter dye
- L8 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN  
TI **Thermal gradient DNA** chip
- L8 ANSWER 12 OF 15 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN  
TI **DNA** Mutation Detection in a Polymer Microfluidic Network Using Temperature Gradient Gel Electrophoresis.
- L8 ANSWER 13 OF 15 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN  
TI Genotyping on a **thermal gradient DNA** chip.
- L8 ANSWER 14 OF 15 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN  
TI Determination of melting temperature for variant detection using dHPLC: A comparison between an empirical approach and **DNA** melting prediction software.
- L8 ANSWER 15 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN  
TI Gradient microfluidic device, for providing linear temperature gradient to substrate, comprises substrate with architecture for parallel chemical or biochemical processing, and first and second temperature elements.

=> d ibib abs 18 1,2,5,8-11,14,15

L8 ANSWER 1 OF 15 MEDLINE on STN  
ACCESSION NUMBER: 2004094095 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 14961715  
TITLE: **DNA** mutation detection in a polymer microfluidic network using temperature gradient gel electrophoresis.  
AUTHOR: Buch Jesse S; Kimball Christopher; Rosenberger Frederick; Highsmith W Edward Jr; DeVoe Don L; Lee Cheng S  
CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of Maryland, College Park, MD 20742, USA.  
CONTRACT NUMBER: CA 092819 (NCI)  
SOURCE: Analytical chemistry, (2004 Feb 15) 76 (4) 874-81.  
Journal code: 0370536. ISSN: 0003-2700.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200408  
ENTRY DATE: Entered STN: 20040302  
Last Updated on STN: 20040806  
Entered Medline: 20040805

AB A miniaturized system for **DNA** mutation analysis, utilizing temperature gradient gel electrophoresis (TGGE) in a polycarbonate (PC) microfluidic device, is reported. TGGE reveals the presence of sequence heterogeneity in a given heteroduplex sample by introducing a **thermal** denaturing **gradient** that results in differences between the average electrophoretic mobilities of **DNA** sequence variants. Bulk heater assemblies are designed and employed to externally generate temperature gradients in spatial and temporal formats along the separation channels. TGGE analyses of model mutant **DNA**

fragments, each containing a single base substitution, are achieved using both single- and 10-channel parallel measurements in a microfluidic platform. Additionally, a comprehensive polymer microfluidic device containing an integrated microheater and sensor **array** is developed and demonstrated for performing spatial TGGE for **DNA** mutation analysis. The device consists of two PC modular substrates mechanically bonded together. One substrate is embossed with microchannels, and the other contains a tapered microheater, lithographically patterned along with an **array** of temperature sensors. Compared with the external heating approaches, the integrated platform provides significant reduction in power requirement and **thermal** response time while establishing more accurate and highly effective control of the temperature **gradient** for achieving improved separation resolution.

L8 ANSWER 2 OF 15 MEDLINE on STN  
ACCESSION NUMBER: 2003105480 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12618377  
TITLE: Genotyping on a **thermal gradient**  
**DNA** chip.  
AUTHOR: Kajiyama Tomoharu; Miyahara Yuji; Kricka Larry J; Wilding Peter; Graves David J; Surrey Saul; Fortina Paolo  
CORPORATE SOURCE: Department of Pediatrics, The Children's Hospital of Philadelphia and University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania 19104, USA.  
CONTRACT NUMBER: P60-HL38632 (NHLBI)  
R21CA83220-01A1 (NCI)  
SOURCE: Genome research, (2003 Mar) 13 (3) 467-75.  
Journal code: 9518021. ISSN: 1088-9051.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200304  
ENTRY DATE: Entered STN: 20030306  
Last Updated on STN: 20030416  
Entered Medline: 20030411  
AB Silicon-based chips with discrete, independently temperature-controlled islands have been developed for use in **DNA microarray** hybridization studies. Each island, containing a heater made of a diffusion layer and a temperature sensor based on a p-n junction, is created on a silicon dioxide/nitride surface by anisotropic etching. Different reactive groups are subsequently added to the surface of the islands, and allele-specific oligonucleotide probes are attached to discrete spots on the chip. Hybridization is performed with Cy5-tagged single-stranded targets derived by PCR from genomic **DNA**. Results are assessed by measuring fluorescence of bound dye-tagged targets after hybridization and washing. Temperatures at each island can be set at different values to obtain optimal distinction between perfect matches and mismatches. This approach facilitates definition of optimal temperatures for probe/target annealing and for distinction between perfectly matched versus mismatched solution-phase targets. The **thermal gradient DNA** chips were then tested for genotyping, and the results for four different loci in two genes are presented. Unambiguous typing was achieved for clinically relevant loci within the factor VII and hemochromatosis genes.

L8 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:756000 CAPLUS  
DOCUMENT NUMBER: 141:237717  
TITLE: Analysis of point mutations by **array**  
hybridization, **thermal gradient**



denaturation and total internal reflection fluorometry  
 PATENT ASSIGNEE(S): Klapproth, Holger, Germany  
 SOURCE: Ger. Offen., 7 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10309526	A1	20040916	DE 2003-10309526	20030304
PRIORITY APPLN. INFO.:			DE 2003-10309526	20030304

AB The invention describes a procedure for identifying point mutation using **DNA** microarrays and stimulation of total internal reflection fluorescence. Target nucleic acids and probes are hybridized at a permissive temperature and hybrids are eluted by increasing the stringency of hybridization by increasing the temperature. Denaturation can be detected by total internal reflection fluorometry and m.p. curves are generated and the difference of the m.p. curves between the probe for the wild type **DNA** and the probe for the appropriate mutant **DNA** is generated. The shape of the melting curve allows clear identification of a homozygotes and heterozygotes.

L8 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:350363 CAPLUS  
 DOCUMENT NUMBER: 138:85835  
 TITLE: Surface modification and hybridization on a **thermal gradient DNA** chip  
 AUTHOR(S): Kajiyama, T.; Sakazume, T.; Miyahara, Y.; Surrey, S.; Graves, D. J.; Wilding, P.; Kricka, L. J.; Fortina, P.  
 CORPORATE SOURCE: Dept Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA, 19104, USA  
 SOURCE: Micro Total Analysis Systems 2001, Proceedings  $\mu$ TAS 2001 Symposium, 5th, Monterey, CA, United States, Oct. 21-25, 2001 (2001), 585-586. Editor(s): Ramsey, J. Michael; Berg, Albert van den. Kluwer Academic Publishers: Dordrecht, Neth.  
 CODEN: 69COT6; ISBN: 1-4020-0148-7  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

AB We developed a method for attaching oligonucleotide (ON) probes to the silicon nitride surface of a **thermal gradient DNA** chip. We verified that aminosilane and polylysine were effective in generating reactive surface amino groups, and phenyl-diisothiocyanate (PDC) was effective to link amino modified ON to the chip surface. We used the chip to detect single-base changes by allele-specific ON hybridization.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD: ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:107220 CAPLUS  
 DOCUMENT NUMBER: 136:147447  
 TITLE: Apparatus for generating a temperature gradient and methods for using the gradient to characterize molecular interactions  
 INVENTOR(S): Blumenfeld, Martin; Fisher, Mark; Williamson, Fred; Cibuzar, Gregory T.; Van Ness, Brian G.  
 PATENT ASSIGNEE(S): Regents of the University of Minnesota, USA  
 SOURCE: PCT Int. Appl., 90 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009868	A2	20020207	WO 2001-US23831	20010730
WO 2002009868	A3	20020627		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 6544477	B1	20030408	US 2000-630172	20000801
US 2002015995	A1	20020207	US 2001-853806	20010511
US 6733729	B2	20040511		
US 2002015996	A1	20020207	US 2001-853964	20010511
US 6610470	B2	20030826		
CA-2417889	AA	20020207	CA 2001-2417889	20010730
EP 1307293	A2	20030507	EP 2001-961792	20010730
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004505255	T2	20040219	JP 2002-515410	20010730
PRIORITY APPLN. INFO.:			US 2000-630172	A 20000801
			WO 2001-US23831	W 20010730

AB A novel apparatus for generating temperature gradients is described. The apparatus includes a semiconductive wafer and elec. connectors attached to, preferably, one of the edges of the wafer. Methods for transferring the temperature gradients to strata are described. The temperature gradients on the strata can be used for analyses of mols., particularly biol. macromols. The present invention also includes improved methods for determining the thermal stability of binding complexes.

L8 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:676314 CAPLUS

DOCUMENT NUMBER: 135:222342

TITLE: A device for detecting specific hybridization in microarrays using temperature gradients and imaging of hybridizations labeled with a reporter dye

INVENTOR(S): Nakao, Motonao; Yamamoto, Kenji; Yoshii, Junji; Mizuno, Katsuya

PATENT ASSIGNEE(S): Hitachi Software Engineering Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 20 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1132485	A2	20010912	EP 2001-105870	20010309
EP 1132485	A3	20031008		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

IE, SI, LT, LV, FI, RO  
 JP 2001255328 A2 20010921 JP 2000-67684 20000310  
 US 2002022226 A1 20020221 US 2001-802804 20010309  
 US 6589740 B2 20030708

PRIORITY APPLN. INFO.: JP 2000-67684 A 20000310

AB The present invention detects and quantitates only specific hybridization bindings. A biochip spotted with a plurality of probe biopolymers is accommodated in a container into which a washing solution is supplied from a liquid supplying unit. A heating block controls the temperature of the biochip according to a predetd. time pattern. An imaging device captures an image of the spot surface of the biochip at predetd. intervals. The plurality of images picked up with the pickup unit are stored in a computer. By analyzing the images for individual spots, hybridization can be detected with high reliability for every spot without being influenced by optimal hybridization temps. which differ depending upon the types of probes on the spots.

L8 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:670656 CAPLUS

DOCUMENT NUMBER: 134:361916

TITLE: Thermal gradient DNA chip

AUTHOR(S): Kajiyama, Tomoharu; Murakawa, Katsuji; Miyahara, Yuji

CORPORATE SOURCE: Life Science Group, Hitachi, Ltd., Tokyo, 185-8601, Japan

SOURCE: Micro Total Analysis Systems 2000, Proceedings of the  $\mu$ TAS Symposium, 4th, Enschede, Netherlands, May 14-18, 2000 (2000), 505-508. Editor(s): Van den Berg, Albert; Olthuis, W.; Bergveld, Piet. Kluwer Academic Publishers: Dordrecht, Neth.

CODEN: 69AJPB

DOCUMENT TYPE: Conference

LANGUAGE: English

AB We have developed a new **DNA** chip that allows the temperature of each **DNA** probe to be controlled independently and set to an optimum value. By simulation, a **thermal gradient** is found to be established in the SiO<sub>2</sub> membrane on the chip. We fabricated the prototype chip and evaluated the fundamental characteristics of the chip. The temperature-sensing characteristic is almost linear, so the Si-islands' temps. can be detected and controlled by using the simple function of the pn-junction's voltage. With the proposed structure, an Si-island can effectively be thermally isolated from the neighboring islands. Using this new **DNA** chip, we can arrange the appropriate **DNA** probes depending on the melting temperature and hybridization between a target **DNA** and carry it out in the optimum condition.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 15 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002414044 EMBASE

TITLE: Determination of melting temperature for variant detection using dHPLC: A comparison between an empirical approach and **DNA** melting prediction software.

AUTHOR: Rudolph J.G.; White S.; Sokolsky C.; Bozak D.; Mazzanti C.; Lipsky R.H.; Goldman D.

CORPORATE SOURCE: Dr. J.G. Rudolph, Transgenomic, Inc., 11 Firstfield Road, Gaithersburg, MD 20878, United States.  
 jrudolph@transgenomic.com

SOURCE: Genetic Testing, (2002) 6/3 (169-176).  
 Refs: 23

ISSN: 1090-6576 CODEN: GETEF4

COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 022 Human Genetics  
027 Biophysics, Bioengineering and Medical Instrumentation  
029 Clinical Biochemistry

LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Detection of **DNA** sequence variants by the use of denaturing high-performance liquid chromatography (dHPLC) is a relatively new method (Underhill et al., 1997) and has distinct advantages over other methods such as single-strand conformation polymorphism (SSCP), direct sequencing, and **DNA** chip hybridization. The dHPLC-based single-nucleotide polymorphism (SNP) screening relies on different **DNA** thermodynamic properties between perfectly matched base pairs in homoduplex molecules and single base-pair mismatches in heteroduplex DNAs. Separation of the two forms of duplex DNAs by dHPLC is based on ionic forces between the negatively charged **DNA** and the hydrophobic stationary phase, which consists of C(18) chains on PS-DVB (polystyrene-divinylbenzene) beads coated with a positively charged ion-pairing agent (TEAA, triethylammonium acetate). Removal of the **DNA** from the TEAA-coated beads is dependent upon a mobile organic phase, in the form of a linear acetonitrile **gradient**. The major factor that influences the success of dHPLC to detect sequence variation is the **thermal** stability of the duplex **DNA**, which is determined by the melting temperature (TM(50)), where 50% of the **DNA** strand is single stranded and 50% is double stranded. The TM(50) predicts the best probability of detecting a single base-pair change based on the altered thermodynamics it imparts to the **DNA** duplex. Generally, there are two ways to determine this melting temperature, either empirically or with the aid of predictive **DNA** melting analysis software. Such programs include the DNAMelt program located on the Stanford University **DNA** Sequencing and Technology Center website, MeltCalc® (Schutz and vonAhsen 1999), and WAVEMAKER®, the proprietary melting analysis software provided with the Transgenomic WAVE® dHPLC system. The goal of the current study was to determine whether currently available predictive **DNA** melting programs could be used to increase efficiency and throughput of SNP detection. A wide range of amplicons, differing in both size and GC composition, were selected for analysis to simulate the broad spectrum of PCR products that may be encountered during a large-scale dHPLC screening project.

L8 ANSWER 15 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN  
ACCESSION NUMBER: 2003-441334 [41] WPIDS  
DOC. NO. CPI: C2003-116803  
TITLE: Gradient microfluidic device, for providing linear temperature gradient to substrate, comprises substrate with architecture for parallel chemical or biochemical processing, and first and second temperature elements.  
DERWENT CLASS: B04 J04  
INVENTOR(S): CREMER, P S; MAO, H; YANG, T  
PATENT ASSIGNEE(S): (CREM-I) CREMER P S; (MAOH-I) MAO H; (YANG-I) YANG T; (TEXA) UNIV TEXAS A & M SYSTEM  
COUNTRY COUNT: 101  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003037514	A2	20030508	(200341)*	EN	38
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU					
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
 RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM  
 ZW

US 2004005720 A1 20040108 (200404)  
 AU 2002359329 A1 20030512 (200464)

# APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003037514	A2	WO 2002-US34754	20021030
US 2004005720	A1 Provisional	US 2001-339904P	20011030
		US 2002-285323	20021030
AU 2002359329	A1	AU 2002-359329	20021030

# FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002359329	A1 Based on	WO 2003037514

PRIORITY APPLN. INFO: US 2001-339904P 20011030; US  
 2002-285323 20021030

AN 2003-441334 [41] WPIDS  
 AB WO2003037514 A UPAB: 20030630

NOVELTY - A **gradient** microfluidic device, for providing a temperature **gradient** to a substrate, comprises a substrate with an architecture for massively parallel chemical or biochemical processing; first and second temperature elements parallel to each other, in **thermal** contact with the substrate, and where the temperature **gradient** is linear.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for simultaneously determining the effect of temperature and at least one other parameter on the crystallization of an analyte, by:

- (1) providing a microfluidic device;
- (2) varying the parameter as a function of position on the substrate (3); and
- (3) providing the first temperature element (1) at a temperature that is different than that of the second temperature element (2), so that a linear temperature gradient (7) is formed between the two elements.

USE - For providing a linear temperature **gradient** to a substrate by **thermally** contacting the substrate with first and second temperature elements that are in parallel (claimed).

ADVANTAGE - The novel system allows thermal equilibrium to be reached very quickly, e.g. as fast as 107 deg. C/s. It affords a convenient, one-shot method of obtaining a melting curve for double stranded DNA.

DESCRIPTION OF DRAWING(S) - The figures show a temperature gradient microfluidic device, and geometry of the channels in the microfluidic device, as above.

First temperature element 1  
 Second temperature element 2  
 Substrate 3  
 Channels 4  
 Temperature gradient 7  
 Cover 8  
 Inlet 9  
 Outlet 10  
 Dwg.1/12

=> (DNA or protein) and perpendicular?

L12 5350 (DNA OR PROTEIN) AND PERPENDICULAR?

=> 16 and perpendicular

L13 261 L6 AND PERPENDICULAR

=> d his

(FILE 'HOME' ENTERED AT 15:21:50 ON 07 FEB 2005)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 15:22:26 ON 07 FEB 2005

E SOGARD M/AU

L1 87 E3-E6

L2 11 L1 AND ?THERM?

L3 8 DUP REM L2 (3 DUPLICATES REMOVED)

L4 1 L3 AND DNA

L5 7 L3 NOT L4

L6 11990 (THERMIC OR THERMAL OR THERMICALLY OR THERMALLY) (S) GRADIENT

L7 90771 (DNA OR PROTEIN) AND (ARRAY OR MICROARRAY)

L8 15 L6 AND L7

L9 1 (THERMOPHORESIS OR THERMOPHORETIC) AND L7

L10 0 L9 NOT L4

L11 15 L8 NOT L4

L12 5350 (DNA OR PROTEIN) AND PERPENDICULAR?

L13 261 L6 AND PERPENDICULAR

=> (THERMIC OR THERMAL OR THERMICALLY OR THERMALLY) (S) GRADIENT (s)perpendicular?

L14 139 (THERMIC OR THERMAL OR THERMICALLY OR THERMALLY) (S) GRADIENT  
(S) PERPENDICULAR?

=> 114 and (DNA or PROTEIN)

L15 12 L14 AND (DNA OR PROTEIN)

=> dup rem 115

PROCESSING COMPLETED FOR L15

L16 8 DUP REM L15 (4 DUPLICATES REMOVED)

=> t ti 116 1-8

L16 ANSWER 1 OF 8 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

TI Thermal gradient apparatus comprises semiconducting wafer, two electrical connectors adjacent to each other on the wafer, and power source connected to the wafer through the connectors.

L16 ANSWER 2 OF 8 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

TI Thermal gradient apparatus used for analysis of biological macromolecules, comprises semiconducting wafer, two adjacent electrical connectors, and power source.

L16 ANSWER 3 OF 8 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

TI Thermal gradient apparatus, useful for analysis of biological macromolecules, comprises semiconducting wafer, two adjacent electrical connectors and power source.

L16 ANSWER 4 OF 8 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

TI The relative stabilities of base pair stacking interactions and single mismatches in long RNA measured by temperature gradient gel electrophoresis.

L16 ANSWER 5 OF 8 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN  
TI The thermal stability of DNA fragments with tandem mismatches at  
a d(CXYG)·d(CY'X'G) site.

L16 ANSWER 6 OF 8 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN  
TI Influence of neighboring base pairs on the stability of single base bulges  
and base pairs in a DNA fragment.

L16 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 1  
TI Influence of nearest neighbor sequence on the stability of base pair  
mismatches in long DNA; determination by temperature-gradient  
gel electrophoresis.

L16 ANSWER 8 OF 8 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN  
TI Producing suitable temperature gradient for gel layer - on thermally conductive  
plate with heated and cooled opposite edges, useful in bio-technological  
assays etc..

=> d ibib abs 116 1-8

L16 ANSWER 1 OF 8 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN  
ACCESSION NUMBER: 2002-339267 [37] WPIDS  
CROSS REFERENCE: 2002-225941 [28]; 2002-328525 [36]; 2003-775976 [73]  
DOC. NO. CPI: C2002-097355  
TITLE: Thermal gradient apparatus comprises semiconducting  
wafer, two electrical connectors adjacent to each other  
on the wafer, and power source connected to the wafer  
through the connectors.  
DERWENT CLASS: A89 B04 D16  
INVENTOR(S): BLUMENFELD, M; CIBUZAR, G T; FISHER, M; VAN NESS, B G;  
WILLIAMSON, F  
PATENT ASSIGNEE(S): (MINU) UNIV MINNESOTA  
COUNTRY COUNT: 96  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002009868	A2	20020207	(200237)*	EN	90
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2001083031	A	20020213	(200238)		
EP 1307293	A2	20030507	(200332)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
JP 2004505255	W	20040219	(200414)		129

# APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002009868	A2	WO 2001-US23831	20010730
AU 2001083031	A	AU 2001-83031	20010730
EP 1307293	A2	EP 2001-961792	20010730
		WO 2001-US23831	20010730
JP 2004505255	W	WO 2001-US23831	20010730

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001083031	A Based on	WO 2002009868
EP 1307293	A2 Based on	WO 2002009868
JP 2004505255	W Based on	WO 2002009868

PRIORITY APPLN. INFO: US 2000-630172 20000801

AN 2002-339267 [37] WPIDS

CR 2002-225941 [28]; 2002-328525 [36]; 2003-775976 [73]

AB WO 200209868 A UPAB: 20040226

NOVELTY - Thermal gradient apparatus comprises a semiconducting wafer (110), two electrical connectors (114a-b) adjacent to each other on the wafer, and a power source connected to the wafer through the connectors. Each connector is attached to the wafer at an attachment site with a gap disposed between the two attachment sites.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(A) a method of generating a temperature gradient, which comprises attaching two electrical connectors to a semiconducting wafer, and connecting a power source to the wafer through the connectors;

(B) a method of analyzing biological macromolecules or assessing binding complex interactions, which comprises establishing a temperature gradient on a semiconducting wafer having a stratum disposed upon it, where the stratum has at least one sample comprising biological macromolecules or comprising at least one member of a binding complex in thermal contact with the temperature gradient and the wafer has two connectors connected to opposite poles of an electrical power source; and evaluating the samples by measuring a property of the sample to determine thermal stability of complexes formed with the biological macromolecules in the samples or to determined thermal stability of the binding complex on the stratum; and

(C) a method of conducting nucleic acid hybridization, which comprises establishing a temperature gradient, and performing a hybridization protocol on the samples to determine temperature effect based on the gradient.

USE - The apparatus is used for generating a temperature gradient useful in molecular interactions, particularly for characterizing interactions involving biological macromolecules.

ADVANTAGE - The inventive apparatus provides a shallow linear temperature gradient. The temperature gradient produced can be transferred successively through the lucite base of the fluidic cell, a glass slide, an acrylamide gel and another glass slide, the fluid film covering the glass slide and the lucite lid of the fluidic cell.

DESCRIPTION OF DRAWING(S) - The figure is a top view of a thermal gradient apparatus.

Wafer 110

Electrical connectors 114a-b

Dwg.1/11

L16 ANSWER 2 OF 8 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-328525 [36] WPIDS

CROSS REFERENCE: 2002-225941 [28]; 2002-339267 [37]; 2003-775976 [73]

DOC. NO. NON-CPI: N2002-257793

DOC. NO. CPI: C2002-094840

TITLE: Thermal gradient apparatus used for analysis of biological macromolecules, comprises semiconducting wafer, two adjacent electrical connectors, and power source.

DERWENT CLASS: A89 B04 D16 S03



INVENTOR(S): BLUMENFELD, M; CIBUZAR, G T; FISHER, M; NESS, B G V;  
 WILLIAMSON, F; VAN NESS, B G  
 PATENT ASSIGNEE(S): (BLUM-I) BLUMENFELD M; (CIBU-I) CIBUZAR G T; (FISH-I)  
 FISHER M; (NESS-I) NESS B G V; (WILL-I) WILLIAMSON F;  
 (MINU) UNIV MINNESOTA  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002015996	A1	20020207	(200236) *		45
US 6610470	B2	20030826	(200357)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002015996	A1 Div ex	US 2000-630172	20000801
		US 2001-853964	20010511
US 6610470	B2 Div ex	US 2000-630172	20000801
		US 2001-853964	20010511

PRIORITY APPLN. INFO: US 2000-630172 20000801; US  
 2001-853964 20010511

AN 2002-328525 [36] WPIDS  
 CR 2002-225941 [28]; 2002-339267 [37]; 2003-775976 [73]  
 AB US2002015996 A UPAB: 20031112

NOVELTY - A thermal gradient apparatus comprising a semiconducting wafer, two adjacent electrical connectors on the wafer, and a power source, where each of the connectors are attached to the wafer at an attachment site, a gap is disposed between the two attachment sites and a power source is connected to the wafer through the electrical connectors, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) generating a temperature gradient comprising the thermal gradient apparatus;

(2) analyzing biological macromolecules comprising establishing a temperature gradient on a semiconducting wafer having a stratum disposed on it, where the stratum has one or more samples comprising biological macromolecules in thermal contact with the temperature gradient and evaluating the samples to determine thermal stability of the complexes formed with the biological macromolecules in the samples, where the samples are evaluated by measuring a property of the sample;

(3) conducting nucleic acid hybridization comprising establishing a temperature gradient on a semiconducting wafer having a stratum disposed on it, where the stratum has one or more samples comprising nucleic acid molecules in thermal contact with the temperature gradient and performing a hybridization protocol on the samples to determine temperature effect based on the gradient; and

(4) assessing binding complex interactions comprising establishing a temperature gradient on a semiconducting wafer having a stratum disposed on it, where the stratum has one or more samples comprising members of binding complexes in thermal contact with the temperature gradient and evaluating the samples to determine thermal stability of the binding complex on the stratum.

USE - For use in generating temperature gradient useful for the analysis of molecules, preferably biological macromolecules.

ADVANTAGE - The inventive apparatus is able to generate stable temperature gradient.

DESCRIPTION OF DRAWING(S) - The figure is a schematic diagram of the thermal gradient apparatus.

Semiconducting wafer 110  
 Electrical connectors 114a, 114b  
 Electrical wires 116a, 116b  
 Electrical transformer 120  
 Power source 126  
 Temperature sensor 130  
 Gap 134  
 Temperature controller 136  
 Relay switch 140  
 Dwg.1/11

L16 ANSWER 3 OF 8 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2002-225941 [28] WPIDS  
 CROSS REFERENCE: 2002-328525 [36]; 2002-339267 [37]; 2003-775976 [73]  
 DOC. NO. NON-CPI: N2002-173337  
 DOC. NO. CPI: C2002-068793  
 TITLE: Thermal gradient apparatus, useful for analysis of  
 biological macromolecules, comprises semiconducting  
 wafer, two adjacent electrical connectors and power  
 source.  
 DERWENT CLASS: B04 D16 T01 U11  
 INVENTOR(S): BLUMENFELD, M; CIBUZAR, G T; FISHER, M; VAN NESS, B G;  
 WILLIAMSON, F  
 PATENT ASSIGNEE(S): (BLUM-I) BLUMENFELD M; (CIBU-I) CIBUZAR G T; (FISH-I)  
 FISHER M; (VNES-I) VAN NESS B G; (WILL-I) WILLIAMSON F;  
 (MINU) UNIV MINNESOTA  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US-2002015995	A1	20020207	(200228)*		45
US 6733729	B2	20040511	(200431)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002015995	A1 Div ex	US 2000-630172	20000801
		US 2001-853806	20010511
US 6733729	B2 Div ex	US 2000-630172	20000801
		US 2001-853806	20010511

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6733729	B2 Div ex	US 6544477

PRIORITY APPLN. INFO: US 2000-630172 20000801; US  
 2001-853806 20010511

AN 2002-225941 [28] WPIDS  
 CR 2002-328525 [36]; 2002-339267 [37]; 2003-775976 [73]  
 AB US2002015995 A UPAB: 20040514

NOVELTY - A thermal gradient apparatus comprising a semiconducting wafer,  
 two adjacent electrical connectors on the wafer, and a power source, where  
 each of the connectors is attached to the wafer at an attachment site, a  
 gap is disposed between the two attachment sites and the power source is  
 connected to the wafer through the electrical connectors, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the  
 following:

(1) generating a temperature gradient;

(2) analyzing (M1) biological macromolecules comprising establishing a temperature gradient using the thermal gradient apparatus and evaluating the samples to determine thermal stability of complexes formed with the biological macromolecules in the samples, where the samples are evaluated by measuring a property of the sample;

(3) conducting nucleic acid hybridization comprising establishing a temperature gradient using the thermal gradient apparatus and performing a hybridization protocol on the sample to determine temperature effect based on the gradient; and

(4) assessing binding complex interactions comprising establishing a temperature gradient using the thermal gradient apparatus and evaluating the samples to determine thermal stability of the binding complex on the stratum.

USE - For use in generating temperature gradient useful for the analysis of molecules, preferably biological macromolecules.

ADVANTAGE - The inventive apparatus is able to generate stable temperature gradient.

DESCRIPTION OF DRAWING(S) - The figure is a schematic diagram of the thermal gradient apparatus.

Semiconducting wafer 110  
Electrical connectors 114a, 114b  
Electrical wires 116a, 116b  
Electrical transformer 120  
Power source 126  
Temperature sensor 130  
Gap 134  
Temperature controller 136  
Relay switch 140  
Dwg.1/11

L16 ANSWER 4 OF 8 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 97384057 EMBASE

DOCUMENT NUMBER: 1997384057

TITLE: The relative stabilities of base pair stacking interactions and single mismatches in long RNA measured by temperature gradient gel electrophoresis.

AUTHOR: Zhu J.; Wartell R.M.

CORPORATE SOURCE: R.M. Wartell, School of Biology, Georgia Institute of Technology, Atlanta, GA 30332, United States

SOURCE: Biochemistry, (1997) 36/49 (15326-15335).

Refs: 29

ISSN: 0006-2960 CODEN: BICHAW

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The **thermal** stability of RNA duplexes differing by a single base pair (bp) substitution or mismatch were investigated by temperature **gradient** gel electrophoresis (TGGE). All base pair substitutions and mismatches were examined at six sites, and limited changes were investigated at three other sites. **DNA** templates for in vitro transcription were generated by the polymerase chain reaction (PCR). Transcribed forward and reverse single stranded RNAs were annealed to form 345 bp duplex RNA. Solution melting curves of selected RNAs were in good agreement with the predicted three step transitions. Parallel TGGE was used to determine the relative stabilities of the RNAs, and **perpendicular** TGGE was employed to obtain mobility transitions and midpoint transition temperatures ( $T(\mu)$ ) of the RNAs' first melting domain. The gel solvent included formamide and urea. The  $T(\mu)$  values of the first melting domain were influenced by the identity of the base pair

substitution or mismatch as well as by the site's neighboring base pairs. The difference in the transition temperatures ( $\delta T(\mu)$ ) between pairs of RNA ranged from 0 to 5 °C.  $\delta T\mu$  values were used to determine free energy differences ( $\delta\Delta G$ ). For RNA pairs distinguished by a base pair substitution, the  $\delta\Delta G$  values were closely correlated with free energy differences calculated from stacking free energies determined from melting studies in 1 M Na<sup>+</sup> [Serra, M. J., and Turner, D. H. (1995) *Methods Enzymol.* 259, 242-261.] An algorithm was developed using the free energies of terminal mismatches [Serra, M. J., and Turner, D. H. (1995) *Methods Enzymol.* 259, 242-261] that provided very good agreement with experimental free energies for the single internal mismatches.

L16 ANSWER 5 OF 8 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 96090680 EMBASE  
DOCUMENT NUMBER: 1996090680  
TITLE: The thermal stability of DNA fragments with tandem mismatches at a d(CXYG)·d(CY'X'G) site.  
AUTHOR: Ke S.-H.; Wartell R.M.  
CORPORATE SOURCE: School of Biology, Georgia Institute of Technology, Atlanta, GA 30332, United States  
SOURCE: Nucleic Acids Research, (1996) 24/4 (707-712).  
ISSN: 0305-1048 CODEN: NARHAD  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Temperature-Gradient Gel Electrophoresis (TGGE) was employed to determine the **thermal** stabilities of 28 DNA fragments, 373 bp long, with two adjacent mismatched base pairs, and eight DNAs with Watson-Crick base pairs at the same positions. Heteroduplex DNAs containing two adjacent mismatches were formed by melting and reannealing pairs of homologous 373 bp DNA fragments differing by two adjacent base pairs. Product DNAs were separated based on their **thermal** stability by parallel and **perpendicular** TGGE. The polyacrylamide gel contained 3.36 M urea and 19.2% formamide to lower the DNA melting temperatures. The order of stability was determined in the sequence context d(CXYG)·d(CY'X'G) where X·X' and Y·Y' represent the mismatched or Watson-Crick base pairs. The identity of the mismatched bases and their stacking interactions influence DNA stability. Mobility transition melting temperatures (T(U)) of the DNAs with adjacent mismatches were 1.0-3.6°C (±0.2°C) lower than the homoduplex DNA with the d(CCAG)·d(CTGG) sequence. Two adjacent G·A pairs, d(CGAG)·d(CGAG), created a more stable DNA than DNAs with Watson-Crick A·T pairs at the same sites. The d(GA)·d(GA) sequence is estimated to be 0.4 (±30%) kcal/mol more stable in free energy than d(AA)·d(TT) base pairs. This result confirms the unusual stability of the d(GA)·d(GA) sequence previously observed in DNA oligomers. All other DNAs with adjacent mismatched base pairs were less stable than Watson-Crick homoduplex DNAs. Their relative stabilities followed an order expected from previous results on single mismatches. Two homoduplex DNAs with identical nearest neighbor sequences but different next-nearest neighbor sequences had a small but reproducible difference in T(U) value. This result indicates that sequence dependent next neighbor stacking interactions influence DNA stability.

L16 ANSWER 6 OF 8 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 95120660 EMBASE

DOCUMENT NUMBER: 1995120660  
 TITLE: Influence of neighboring base pairs on the stability of single base bulges and base pairs in a DNA fragment.  
 AUTHOR: Ke S.-H.; Wartell R.M.  
 CORPORATE SOURCE: School of Biology, Georgia Institute of Technology, Atlanta, GA 30332, United States  
 SOURCE: Biochemistry, (1995) 34/14 (4593-4600).  
 ISSN: 0006-2960 CODEN: BICHAW  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 029 Clinical Biochemistry  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB Temperature-gradient gel electrophoresis (TGGE) was used to determine the relative thermal stabilities of 32 DNA fragments that differ by a single unpaired base (base bulge) and 17 DNAs differing by a base pair. Homologous 373 and 372 bp DNA fragments differing by a single base pair substitution or deletion were employed. Heteroduplexes containing a single base bulge were formed by melting and reannealing pairs of 372 and 373 bp DNAs. Product DNAs were separated on the basis of their thermal stability by parallel and perpendicular TGGE. The order of stability was determined for all single unpaired bases in four different nearest neighbor environments: (GXT)·(AYC), (GXG)·(CYC), (CXA)·(TYG), and (TXT)·(AYA) with X = A, T, G, or C, and Y = no base, or visa versa. DNA fragments containing a base bulge were destabilized by 2-3.6 °C (±0.2 °C) with respect to homologous DNAs with complete Watson-Crick base pairing. Both the identity of the unpaired base and the sequence of the flanking base pairs influenced the degree of destabilization. The range of temperature shift correspond to estimated unfavorable free energies from 2.5 to 4.6 kcal/mol. Purine base bulges were generally not as destabilizing as pyrimidine base bulges. An unpaired base which was identical to one of its adjacent bases generally caused less destabilization than an unpaired base with an identity differing from its nearest neighbors. This implies that positional degeneracy of an unpaired base within a run of two or more identical bases is an important factor effecting stability. The ability of TGGE to order the stabilities of DNA fragments differing by a single base pair was used to determine the relative stabilities of base pair stacking interactions. The results determined by TGGE were consistent with the relative stabilities determined from UV melting transitions.

L16 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 1  
 ACCESSION NUMBER: 94077716 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 8255768  
 TITLE: Influence of nearest neighbor sequence on the stability of base pair mismatches in long DNA; determination by temperature-gradient gel electrophoresis.  
 AUTHOR: Ke S H; Wartell R M  
 CORPORATE SOURCE: School of Biology, Georgia Institute of Technology, Atlanta 30332.  
 CONTRACT NUMBER: GM38045 (NIGMS)  
 SOURCE: Nucleic acids research, (1993 Nov 11) 21 (22) 5137-43.  
 Journal code: 0411011. ISSN: 0305-1048.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199401  
 ENTRY DATE: Entered STN: 19940203  
 Last Updated on STN: 19940203

Entered Medline: 19940113

AB Temperature-gradient gel electrophoresis (TGGE) was employed to determine the thermal stabilities of 48 DNA fragments that differ by single base pair mismatches. The approach provides a rapid way for studying how specific base mismatches effect the stability of a long DNA fragment. Homologous 373 bp DNA fragments differing by single base pair substitutions in their first melting domain were employed. Heteroduplexes were formed by melting and reannealing pairs of DNAs, one of which was 32P-labeled on its 5'-end. Product DNAs were separated based on their thermal stability by parallel and perpendicular temperature-gradient gel electrophoresis. The order of stability was determined for all common base pairs and mismatched bases in four different nearest neighbor environments; d(GXT).d(AYC), d(GXG).d(CYC), d(CXA).d(TYG), and d(TXT).d(AYA) with X,Y = A, T, C, or G. DNA fragments containing a single mismatch were destabilized by 1 to 5 degrees C with respect to homologous DNAs with complete Watson-Crick base pairing. Both the bases at the mismatch site and neighboring stacking interactions influence the destabilization caused by a mismatch. G.T, G.G and G.A mismatches were always among the most stable mismatches for all nearest neighbor environments examined. Purine.purine mismatches were generally more stable than pyrimidine.pyrimidine mispairs. Our results are in very good agreement with data where available from solution studies of short DNA oligomers.

L16 ANSWER 8 OF 8 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 1988-001232 [01] WPIDS

DOC. NO. NON-CPI: N1988-001014

DOC. NO. CPI: C1988-000520

TITLE: Producing suitable temperature gradient for gel layer - on thermally conductive plate with heated and cooled opposite edges, useful in bio-technological assays etc..

DERWENT CLASS: B04 J04 S03

INVENTOR(S): RIESNER, D; ROSENBAUM, V

PATENT ASSIGNEE(S): (QIAG-N) QIAGEN GMBH; (DIAG-N) DIAGEN INST MOLEK;  
(DIAG-N) DIAGEN INST MOLEKULARBIOLOGISC

COUNTRY COUNT: 11

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 251306	A	19880107	(198801)*	GE	9
R: CH DE FR GB LI LU NL SE					
DE 3622591	A	19880114	(198803)		
JP 63027744	A	19880205	(198811)		
US 5066377	A	19911119	(199149)		9
EP 251306	B1	19921021	(199243)	GE	9
R: BE CH FR GB LI LU NL SE					
JP 07054315	B2	19950607	(199527)		5
DE 3622591	C2	19981119	(199850)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 251306	A	EP 1987-109432	19870701
DE 3622591	A	DE 1986-3622591	19860704
JP 63027744	A	JP 1987-167673	19870703
US 5066377	A	US 1990-545111	19900629
EP 251306	B1	EP 1987-109432	19870701
JP 07054315	B2	JP 1987-167673	19870703
DE 3622591	C2	DE 1986-3622591	19860704

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 07054315	B2 Based on	JP 63027744

PRIORITY APPLN. INFO: DE 1986-3622591 19860704

AN 1988-001232 [01] WPIDS

AB EP 251306 A UPAB: 19930923

A temperature **gradient** applicable to materials held in a separation medium layer, e.g. of gel, and with at least one component undergoing **thermal** conversion, is controllably and reproducibly produced in a **thermally** conductive layer support plate (1) whose one edge (2) contacts one or more adjustable heaters (4), while the opposite edge contacts cooling devices (5). Energy flow of heaters and coolers exceeds energy flow through the plate, which exceeds **perpendicular** energy flow through the supported separation medium. Both heating and cooling may derive from thermostatically controlled liquid baths. Alternative heaters include electrical resistance wires or Peltier elements.

Plate dimensions may match a commercially available electrophoresis unit.

USE/ADVANTAGE - Claimed for detection and separation of vivoids, vival nuclei acids, or satellite RNAs or for analysis of mutations in nucleic acids, proteins, or **protein**-nucleic acid complexes.

3/3

ABEQ EP 251306 B UPAB: 19930923

A method for producing a controllable and reproducible temperature gradient in a two-dimensional separating medium for the separation of mixtures of substances, wherein the two-dimensional separating medium is located on a heat-conducting plate, characterized in that one single heat-conducting plate (1) is employed and the surface turned away from the heat-conductive plate (1) of the separating medium has been provided with a heat-insulating cover (10), wherein one edge of the plate is heated by means of one or more controllable heating devices (4) and the opposite edge of the plate (1) is cooled by means of one or more controllable cooling devices (5).

1/3

ABEQ US 5066377 A UPAB: 19930923

Electrophoresis device comprises a sheet-shaped sepg. medium in which a linear controllable temp. gradient can be reproduced by a single heat conducting plate opposed to the first surface of the sepg. medium and a controllable heater for heating one edge of the plate. A cooler cools the opposite edge of the plate. An insulator is opposed to the other surface of the sepg. medium.

ADVANTAGE - Low cost device.

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(FILE 'HOME' ENTERED AT 15:21:50 ON 07 FEB 2005)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 15:22:26 ON 07 FEB 2005

E SOGARD M/AU

L1	87 E3-E6
L2	11 L1 AND ?THERM?
L3	8 DUP REM L2 (3 DUPLICATES REMOVED)
L4	1 L3 AND DNA
L5	7 L3 NOT L4
L6	11990 (THERMIC OR THERMAL OR THERMICALLY OR THERMALLY) (S) GRADIENT
L7	90771 (DNA OR PROTEIN) AND (ARRAY OR MICROARRAY)

L8           15 L6 AND L7  
 L9           1 (THERMOPHORESIS OR THERMOPHORETIC) AND L7  
 L10          0 L9 NOT L4  
 L11          15 L8 NOT L4  
 L12          5350 (DNA OR PROTEIN) AND PERPENDICULAR?  
 L13          261 L6 AND PERPENDICULAR  
 L14          139 (THERMIC OR THERMAL OR THERMICALLY OR THERMALLY) (S) GRADIENT (  
 L15          12 L14 AND (DNA OR PROTEIN)  
 L16          8 DUP REM L15 (4 DUPLICATES REMOVED)

=> logoff hold

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
172.45	172.66

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-4.38	-4.38

CA SUBSCRIBER PRICE

SESSION WILL BE HELD FOR 60 MINUTES  
 STN INTERNATIONAL SESSION SUSPENDED AT 15:46:11 ON 07 FEB 2005